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? SHOW FILES
File 155:MEDLINE(R) 1951-2005/Nov 11
         (c) format only 2005 Dialog
File   5:Biosis Previews(R) 1969-2005/Nov W1
         (c) 2005 BIOSIS
File  34:SciSearch(R) Cited Ref Sci 1990-2005/Nov W1
         (c) 2005 Inst for Sci Info
File  71:ELSEVIER BIOBASE 1994-2005/Nov W2
         (c) 2005  Elsevier Science B.V.
File  73:EMBASE 1974-2005/Nov 14
         (c) 2005 Elsevier Science B.V.
File 351:Derwent WPI 1963-2005/UD,UM &UP=200572
         (c) 2005  Thomson Derwent
File 357:Derwent Biotech Res. _1982-2005/Nov W2
         (c) 2005 Thomson Derwent & ISI
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Set     Items   Description
S1         15   SHIGM22 OR LYM22 OR LIM22 OR (LIM OR LYM OR SHIGM OR HIGM)-
              (W)22
S2          9   RD (unique items)
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?
? T S2/3 AB/1-9

 2/AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2005 Dialog. All rts. reserv.
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15095201 PMID: 14655764

Human monoclonal IgM antibody promotes CNS myelin repair independent of Fc function.

Ciric Bogoljub; Howe Charles L; Paz Soldan Mateo; Warrington Arthur E; Bieber Allan J; Van Keulen Virginia; Rodriguez Moses; Pease Larry R

Department of Immunology, Mayo Medical and Graduate Schools, Mayo Clinic Rochester, Minn 55905, USA.

Brain pathology (Zurich, Switzerland) (Switzerland) Oct 2003, 13 (4) p608-16, ISSN 1015-6305 Journal Code: 9216781

Contract/Grant No.: R01 NS24180; NS; NINDS

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

The human monoclonal IgM antibody **sHIgM22** and mouse IgM monoclonal antibody 94.03 bind to oligodendrocytes, induce calcium signals in cultured glial cells, and promote remyelination in mouse models of multiple sclerosis. In order to address the mechanisms employed by these antibodies to promote CNS repair, bivalent monomers, F(ab')2 fragments, and monovalent forms of these antibodies were investigated to determine whether they exhibit the same remyelinating potential as the intact IgMs. The two antibodies displayed different structural requirements for retention of function. Antibody **sHIgM22** remained functional even when reduced to a bivalent F(ab')2 fragment, while disruption of the pentameric structure of antibody 94.03 destroyed its functional properties. Competition studies demonstrated that the two antibodies recognize different entities on the surface of glial cells. These results indicate that the constant region and pentameric structure of IgM is not always necessary for the stimulation of

myelin repair, eliminating the requirement for IgM immune effector functions in this process. The ability of the antibodies to cross-link cell surface determinants on oligodendrocytes appears to be an essential aspect of the mechanism of cellular activation. The finding that two antibodies, which induce similar in vivo effects, bind to different structures, and have different cross-linking requirements suggests that activation of glial cells involves the rearrangement of a complex membrane compartment.

2/AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

14083557 PMID: 11857682
Human antibodies accelerate the rate of remyelination following lysolecithin-induced demyelination in mice.
Bieber Allan J; Warrington Arthur; Asakura Kuni; Ciric Bogoljub; Kaveri Srini V; Pease Larry R; Rodriguez Moses
Department of Neurology, Mayo Medical and Graduate Schools, Rochester, Minnesota 55905, USA. bieber.allan@mayo.edu
Glia (United States) Mar 1 2002, 37 (3) p241-9, ISSN 0894-1491
Journal Code: 8806785
Contract/Grant No.: NS24180; NS; NINDS
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Immunoglobulin-based therapies are becoming increasingly common for the treatment of neurologic and autoimmune diseases in humans. In this study, we demonstrate that systemic administration of either polyclonal human immunoglobulins or specific human monoclonal antibodies can accelerate the rate of CNS remyelination following toxin-induced demyelination. Injection of lysolecithin directly into the spinal cord results in focal demyelinated lesions. In contrast to other murine models of demyelinating disease, the mechanism of demyelination following lysolecithin injection is independent of immune system activation, and chronic inflammation at the site of the lesion is minimal. Administration of polyclonal human IgM (pHIgM) or a serum-derived human monoclonal antibody (**sHIgM22**) resulted in approximately a twofold increase in remyelinating axons when compared to animals treated with saline or with antibodies that do not promote repair. Both pHIgM and **sHIgM22** show strong binding to CNS white matter and oligodendrocytes, while antibodies that did not accelerate remyelination do not. This differential staining pattern suggests that enhanced remyelination may result from direct stimulation of oligodendrocyte remyelination by binding to surface receptors on oligodendrocytes or glial progenitor cells. We propose the use of human polyclonal IgM or specific human monoclonal IgM antibodies as potential therapies to enhance myelin repair following CNS injury and disease. Copyright 2002 Wiley-Liss, Inc.

2/AB/3 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0004486714 BIOSIS NO.: 198529015613
LYM-22 WHICH DEFINES T SUPPRESSORS IS PRESENT ON T HELPER PRECURSORS
AUTHOR: CHAN M (Reprint); TADA N; HAMMERLING U; STUTMAN O
AUTHOR ADDRESS: MEMORIAL SLOAN-KETTERING CANCER CENTER, NEW YORK, NY 10021,

USA**USA
JOURNAL: Federation Proceedings 44 (3): p788 1985
CONFERENCE/MEETING: 69TH ANNUAL MEETING OF THE FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY, ANAHEIM, CALIF., USA, APR. 21-26, 1985. FED PROC.
ISSN: 0014-9446
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH

2/AB/4 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

12631853 EMBASE No: 2004228579
Neuron-binding human monoclonal antibodies support central nervous system neurite extension
Warrington A.E.; Bieber A.J.; Van Keulen V.; Ciric B.; Pease L.R.; Rodriguez M.
Dr. A.E. Warrington, Department of Neurology, Guggenheim 401, Mayo Clinic College of Medicine, 200 First St. SW, Rochester, MN 55905 United States

AUTHOR EMAIL: warrington.arthur@mayo.edu
Journal of Neuropathology and Experimental Neurology (J. NEUROPATHOL. EXP. NEUROL.) (United States) 2004, 63/5 (461-473)
CODEN: JNENA ISSN: 0022-3069
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 62

Two human IgMs (sHIgM12 and sHIgM42) were identified that supported in vitro central nervous system (CNS) neurite extension equal to the potent neurite stimulatory molecule laminin. Both IgMs bound to multiple cell types in unfixed CNS tissue and to the surface of neurons in culture. Both monoclonal antibodies (mAbs) overrode the inhibitory effect of CNS mouse myelin on granule cell neurite extension. Neither mAb bound to the surface of mature oligodendrocytes or strictly colocalized with myelin proteins. Sialidase treatment eliminated the neuronal surface binding of both mAbs, whereas blocking sphingolipid synthesis with Fumonisin B, or removing GP1-linked proteins with PIPLC did not. When used as substrates for mixed neuron/glia aggregates, sHIgM12 and sHIgM42 supported robust neurite extension while astrocytes remained in the aggregates. In contrast, laminin supported astrocyte migration and spreading. Human mAbs that support neurite extension are novel factors that may be of use in encouraging axon repair following injury while minimizing glial cell infiltration. Both human mAbs were isolated from individuals with monoclonal gammopathy. Each individual has carried high mAb titers in circulation for years without detriment. sHIgM12 and sHIgM42 are therefore unlikely to be systemically pathogenic.

2/AB/5 (Item 1 from file: 351)
DIALOG(R)File 351:Derwent WPI

016715686
WPI Acc No: 2005-039961/200504
XRAM Acc No: C05-013422
Composition for promoting CNS remyelination or for treating demyelinating

diseases comprises a recombinant human monoclonal antibody that promotes CNS remyelination
Patent Assignee: ACORDA THERAPEUTICS (ACOR-N); MAYO FOUND MEDICAL EDUCATION & RES (MAYO-N)
Inventor: BIEBER A J; CHOJNICKI E; GRUSKIN E A; RODRIGUEZ M; WARRINGTON A E
Number of Countries: 108 Number of Patents: 001
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 2004110355	A2	20041223	WO 2004US15436	A	20040517	200504	B

Priority Applications (No Type Date): US 2003471235 P 20030516
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 2004110355	A2	E	67	A61K-000/00	

Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
Designated States (Regional): AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

Abstract (Basic): WO 2004110355 A2
Abstract (Basic):

NOVELTY - A pharmaceutical composition comprises a human monoclonal antibody selected from mAb **sHIgM22** (**LYM 22**), sHIgM46 (LYM46), ebvHIgM MSI19D10, Cb2BG8, MSI10E10, their mixtures, monomers, active fragments, binding partners, and recombinant antibodies derived from them, and a pharmaceutical carrier, vehicle or diluent.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) stimulating remyelination of central nervous system (CNS) axons in a mammal; and

(2) treating or preventing a demyelinating disease of the CNS in a mammal.

ACTIVITY - CNS-Gen. No biological data given.

MECHANISM OF ACTION - Gene therapy.

USE - The composition and methods are useful for promoting CNS remyelination or for treating demyelinating diseases as well as other CNS diseases that are of viral, bacterial or idiopathic origin, including neural dysfunction caused by spinal cord injury.

pp; 67 DwgNo 0/6

2/AB/6 (Item 2 from file: 351)
DIALOG(R)File 351:Derwent WPI

015961378
WPI Acc No: 2004-119219/200412
Related WPI Acc No: 1995-393077; 2003-238294
XRAM Acc No: C04-047932
XRPX Acc No: N04-095235
New human immunoglobulin M antibody for treating or preventing a demyelinating disease of the central nervous system in a human or domestic animal, such as multiple sclerosis
Patent Assignee: MAYO FOUND (MAYO-N)
Inventor: MILLER D J; PEASE L R; RODRIGUEZ M
Number of Countries: 001 Number of Patents: 001

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
US 20030185827	A1	20031002	US 94236520	A	19940429	200412 B
			US 96692084	A	19960808	
			US 97779784	A	19970107	
			US 99322862	A	19990528	
			US 2000580787	A	20000530	
			US 2000730473	A	20001205	
			US 200110729	A	20011113	

Priority Applications (No Type Date): US 200110729 A 20011113; US 94236520 A 19940429; US 96692084 A 19960808; US 97779784 A 19970107; US 99322862 A 19990528; US 2000580787 A 20000530; US 2000730473 A 20001205

Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
US 20030185827	A1		159	A61K-039/395	CIP of application US 94236520 Cont of application US 96692084 CIP of application US 97779784 CIP of application US 99322862 CIP of application US 2000580787 CIP of application US 2000730473 CIP of patent US 5591629

Abstract (Basic): US 20030185827 A1

Abstract (Basic):

NOVELTY - An antibody (I) produced by injecting an immunocompetent host with an antibody peptide, and harvesting the antibody, where the peptide comprises a sequence (S1) of 113, 110, 124, or 133 amino acids, given in the specification, or active fragments, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) stimulating remyelination of central nervous system (CNS) axons in a mammal comprising administering a monoclonal antibody, or mixtures, monomers, active fragments, or recombinant antibodies derived from it, characterized by their ability to bind structures and cells within the CNS, including oligodendrocytes;

(2) stimulating the proliferation of glial cells in CNS axons in a mammal comprising administering a monoclonal antibody, or mixtures, monomers, active fragments, or recombinant antibodies derived from it, characterized by their ability to bind structures and cells within the CNS;

(3) treating or preventing a demyelinating disease of the CNS in a mammal comprising administering a monoclonal antibody, or mixtures, monomers, active fragments, or recombinant antibodies derived from it, characterized by their ability to bind structures and cells within the CNS, and to stimulate remyelination of axons of the CNS;

(4) stimulating, in vitro, the proliferation of glial cells from mixed cell culture comprising:

(a) culturing a mixed cell culture containing glial cells to proliferate cells;

(b) introducing into the mixed culture, a monoclonal antibody, or mixtures, monomers, active fragments, or recombinant antibodies derived from it, characterized by their ability to bind structures and cells within the CNS, including oligodendrocytes, to produce a monoclonal-treated mixed culture;

(c) maintaining the culture of (b) to allow proliferation of the cells; and

(d) harvesting the glial cells from the mixed culture;

(5) stimulating remyelination of CNS axons in a mammal comprising:

(a) culturing glial cells;

(b) introducing into the cell culture, a monoclonal antibody

capable of stimulating the cells to exhibit a calcium (Ca2+) peak, or mixtures, monomers, active fragments, or recombinant antibodies derived from it, the autoantibodies characterized by their ability to bind structures and cells within the CNS, including oligodendrocytes, to produce a treated glial cell culture;

(c) maintaining the cell culture of (b) for proliferation of treated cellsd) harvesting the treated cells from the culture to obtain glial cells; and

(e) introducing the glial cells of (d) into the CNS of the mammal;

(6) a DNA sequence or degenerate variant of it, which encodes an antibody, or a peptide analog, hapten, or active fragment of it, where the DNA sequence consists of:

(i) a sequence encoding a protein having S1; or

(ii) a sequence that hybridizes to (i);

(7) a recombinant DNA molecule comprising (6);

(8) a probe capable of screening for the antibody, peptide analog, hapten, or active fragment, in alternate species, prepared from (6);

(9) a unicellular host transformed with (7);

(10) an assay for screening drugs and other agents for the ability to modulate the production or mimic the activities of mAB **sHIgM22** , sHIgM46, or combinations of them, comprising:

(a) culturing an observable cellular test colony inoculated with a drug or agent;

(b) harvesting a supernatant from the colony; and

(c) examining the supernatant for the presence of the mAb, where an increase or decrease indicates the ability of the drug to modulate the activity of the mAb, where the mAb can induce remyelination, bind to neural tissue, promote Ca2+ signaling with oligodendrocytes, and promote cellular proliferation of glial cells;

(11) a test kit for demonstrating the presence of **sHIgM22**, sHIgM46, or combinations comprising the antibody, a specific binding partner of the antibody, other reagents, and directions for use of the kit, where the antibody or specific binding partner are detectably labeled;

(12) a recombinant virus transformed with (7);

(13) a vector comprising (714) a host vector system for the production of a polypeptide which comprises (13) in a host cell;

(15) obtaining a purified polypeptide comprising:

(a) introducing (13) into a host cell;

(b) culturing the cell to produce the polypeptide;

(c) recovering the polypeptide; and

(d) purifying the polypeptide;

(16) imaging a portion of the CNS comprising administering (I), labeled with a detectable label or imaging agent; and

(17) diagnosing or monitoring demyelination and/or remyelination of the CNS comprising using (16).

ACTIVITY - Nootropic; Neuroprotective; Antiviral; Antibacterial; Vulnerary. No suitable biological data is given.

MECHANISM OF ACTION - Cell therapy; Vaccine; Gene therapy.

USE - (I) Is used to stimulate remyelination of CNS axons, and to stimulate the proliferation of glial cells in CNS axons, optionally in vitro. (I) Is used to treat or prevent a demyelinating disease of the CNS in a human or domestic animal, such as multiple sclerosis, or a disease, other injury or dysfunction of the CNS, preferably the mammal is a mouse infected with Strain DA of Theiler's murine encephalomyelitis virus. (I) Is used to treat a spinal cord injury. (I) Is also used to screen drugs and other agents for the ability to modulate the production or mimic the activities of (I). (I) Can be used to image a portion of the CNS which can be used to diagnose or monitor demyelination and/or remyelination of the CNS (all claimed).

pp; 159 DwgNo 0/86

2/AB/7 (Item 3 from file: 351)
DIALOG(R)File 351:Derwent WPI

014245896
WPI Acc No: 2002-066596/200209
XRAM Acc No: C02-019870
XRPX Acc No: N02-049432
Novel neuromodulatory agent (a human IgM monoclonal antibody), promoting neurite outgrowth, regeneration, remyelination and neuroprotection in central nervous system, useful to treat post-infectious encephalomyelitis
Patent Assignee: MAYO FOUND MEDICAL EDUCATION RES (MAYO-N); MAYO FOUND MEDICAL EDUCATION & RES (MAYO-N)
Inventor: MILLER D J; PEASE L R; RODRIGUEZ M
Number of Countries: 094 Number of Patents: 006
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 200185797	A1	20011115	WO 2000US14902	A	20000530	200209	B
AU 200061978	A	20011120	AU 200061978	A	20000530	200219	
EP 1294770	A1	20030326	EP 2000948498	A	20000530	200323	
			WO 2000US14902	A	20000530		
BR 200015875	A	20030624	BR 200015875	A	20000530	200343	
			WO 2000US14902	A	20000530		
JP 2004516807	W	20040610	WO 2000US14902	A	20000530	200438	
			JP 2001582396	A	20000530		
MX 2002011163	A1	20040901	WO 2000US14902	A	20000530	200553	
			MX 200211163	A	20021111		

Priority Applications (No Type Date): US 2000568351 A 20000510
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 200185797	A1	E	219	C07K-016/06	
Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW				
Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW					
AU 200061978	A				Based on patent WO 200185797
EP 1294770	A1	E		C07K-016/06	Based on patent WO 200185797
Designated States (Regional): AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
BR 200015875	A			C07K-016/06	Based on patent WO 200185797
JP 2004516807	W		327	C12N-015/09	Based on patent WO 200185797
MX 2002011163	A1			A61K-039/395	Based on patent WO 200185797

Abstract (Basic): WO 200185797 A1
Abstract (Basic):

NOVELTY - Neuromodulatory agent (I) capable of promoting neurite outgrowth, regeneration, remyelination and neuroprotection in central nervous system (CNS), is new. (I) is human antibody, peptide analog, or hapten. (I) is capable of inducing remyelination, promoting cellular proliferation of glial cells, and promoting calcium ions signaling with oligodendrocytes.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a human or humanized antibody (II) to (I);

(2) an immortal cell line that produces (II);

(3) a DNA sequence or its degenerate variant (III) which encodes an antibody **sHIgM22 (LYM 22)**, ebvHigM MsI19D10, ebv HIgM CB2bG8, AKJR4, CB2iE12, CB2iE7 or MSI19E5, or its peptide analog, a hapten corresponding to antibody, or an active fragment of antibody, having one of 14 11 100-200 nucleotide sequences, all fully defined in the specifications;

(4) a recombinant DNA molecule (IV) comprising (III);

(5) a probe (V) capable of screening for the antibody or its peptide analog, hapten corresponding to antibody, or active fragment of antibody, in alternate species prepared from (III);

(6) a unicellular host (VI) transformed with (IV), where the DNA sequence is operatively linked to an expression control sequence;

(7) detecting (M1) presence or activity of (I), comprising:

(a) contacting a biological sample from a mammal with a binding partner of the neuromodulatory agent; and

(b) detecting if binding has occurred between the neuromodulatory agent from the sample and the binding partner;

(8) detecting the binding sites for (I), comprising:

(a) placing a neuromodulatory agent sample in contact with biological sample from a mammal; and

(b) examining the biological sample in binding studies for the presence of the labeled neuromodulatory agent, where the presence of the label neuromodulatory agent indicates a binding site for a neuromodulatory agent;

(9) testing the ability of a drug to modulate the activity of a neuromodulatory agent, comprisinga) culturing a colony of test cells which has a receptor for the neuromodulatory agent in a growth medium containing the neuromodulatory agent;

(b) adding the drug under test; and

(c) measuring the reactivity of the neuromodulatory agent with the receptor on the colony of test cells;

(10) an assay system for screening drugs for ability to modulate neuromodulatory agent production, or activity, comprising:

(a) culturing an observable cellular test colony inoculated with a drug or agent;

(b) harvesting a supernatant from the colony; and

(c) examining the supernatant for the presence of the neuromodulatory agent, where an increase or a decrease in the level of the neuromodulatory agent indicates a modulator;

(11) a test kit (K1) for the demonstration of a neuromodulatory agent in a eukaryotic cellular sample, comprises a detectably labeled specific binding partner of a neuromodulatory agent;

(12) a test kit (K2) for demonstrating the presence of a neuromodulatory agent in a eukaryotic cellular sample comprises a neuromodulatory agent, a specific binding partner of the neuromodulatory agent, other reagents, and directions for use;

(13) preventing and/or treating (M2) cellular debilitations, derangements and/or dysfunctions and/or other disease states in mammals including humans, and including such conditions in the CNS, comprising administering (I), or a modulator of the neuromodulatory agent;

(14) an antibody (VIII) produced by injecting (I) into a host;

(15) a recombinant virus transformed with (IV) or its derivative or fragment;

(16) an isolated nucleic acid (IX) comprising (III);

(17) an isolated nucleic acid (X) comprising (IX) operatively linked to a promoter of RNA transcription;

(18) a vector (XI) which comprises (X);

(19) a cell line (XIII) comprising (IX); and

(20) a vaccine (XVI) comprising (XI) and a carrier.

ACTIVITY - Antiparkinsonian; Neuroprotective; Nootropic; Virucide; Vulnerary.

Animals with chronic demyelination induced by Strain DA of Theiler's murine encephalomyelitis (TMEV) received intraperitoneal (IP) injections of purified antibodies in phosphate buffered saline. For TMEV infected animals the injection schedule consists of twice weekly injections of 50 micro-g in 100 ml. The duration of antibody treatment is five weeks. Animals are then sacrificed and spinal cord tissue is processed for morphological. For each different antibody treatment, nine chronically infected, female SJL/J mice were infected with antibody. At the end of the treatment period, six of the animals were perfused and processed for morphometric quantitation of demyelination/remyelination and three were sacrificed for frozen tissue that is used for assessment of axonal integrity. The human monoclonal antibodies **sHIgM 22**, sHIgM46 and ebvHIgM MS119D10 significantly promoted remyelination over other tested human monoclonal IgMs. There are no differences in the areas of myelin pathology between the treatment groups.

MECHANISM OF ACTION - Promotion, stimulation, regeneration and/or remyelination of neurons in central nervous system;

USE - (I) is useful for stimulating remyelination of CNS axons, stimulating proliferation of glial cells in CNS axons, or treating demyelinating disease of CNS in a mammal in need of such therapy. (I) is capable of binding to structures and cells within CNS. (I) is preferably useful for treating a demyelinating disease of central nervous system of a mouse infected with Strain DA of Theiler's murine encephalomyelitis (TMEV) or for treating a human being having multiple sclerosis, or a human or domestic animal with a viral demyelinating disease, or a post-neural disease of CNS. (I) is also useful for an in vitro method of stimulating the proliferation of glial cells from mixed cell culture. (I) is also useful for stimulating remyelination of central nervous system axons in a mammal. (II) is useful for preventing infection by a bacterium, virus or like pathogen that causes demyelination or other neurodegenerative condition in a subject. (XI) is useful for obtaining a polypeptide in purified form by recombinant techniques. (XV) is useful for inducing an immune response in a subject which has been exposed to or infected with a bacterium, a virus, or like pathogen that causes demyelination or other neurodegenerative condition. (XVI) is useful for treating a subject infected with or exposed by a bacterium, virus or like pathogen that causes demyelination or other neurodegenerative condition. (M2) is useful for treating multiple sclerosis, Parkinson's disease, Alzheimer's disease, amyotrophic lateral sclerosis (ALS), a viral demyelinating disease, a disease of the central nervous system, and other conditions in the central nervous system where nerves are damaged as by trauma. (All claimed).

ADVANTAGE - The monoclonal antibodies provide greater affinity for neural tissue and both diagnostic and therapeutic capabilitypp; 219 DwgNo 0/44

2/AB/8 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

0357482 DBR Accession No.: 2005-03186 PATENT
Composition for promoting CNS remyelination or for treating demyelinating diseases comprises a recombinant human monoclonal antibody that promotes CNS remyelination - for central nervous system remyelination, virius and bacterium infection and spinal cord injury prevention,

therapy and gene therapy
AUTHOR: GRUSKIN E A; CHOJNICKI E; WARRINGTON A E; BIEBER A J; RODRIGUEZ M
PATENT ASSIGNEE: MAYO FOUND MEDICAL EDUCATION and RES; ACORDA THERAPEUTICS 2004
PATENT NUMBER: WO 2004110355 PATENT DATE: 20041223 WPI ACCESSION NO.: 2005-039961 (200504)
PRIORITY APPLIC. NO.: US 471235 APPLIC. DATE: 20030516
NATIONAL APPLIC. NO.: WO 2004US15436 APPLIC. DATE: 20040517
LANGUAGE: English
ABSTRACT: DERWENT ABSTRACT: NOVELTY - A pharmaceutical composition comprises a human monoclonal antibody selected from mAb **sHIgM22** (**LYM 22**), sHIgM46 (LYM46), ebvHIgM MSI19D10, Cb2BG8, MSI10E10, their mixtures, monomers, active fragments, binding partners, and recombinant antibodies derived from them, and a pharmaceutical carrier, vehicle or diluent. DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) stimulating remyelination of central nervous system (CNS) axons in a mammal; and (2) treating or preventing a demyelinating disease of the CNS in a mammal. BIOTECHNOLOGY - Preferred Composition: The human recombinant antibody corresponds to or is derived from mAb **SHIgM22** (**LYM22**) or mAb SHIgM46 (LYM46). The composition further includes up to about 1-2 mg of a steroid, the steroid comprising or corresponding to methylprednisolone.Preferred Methods: Stimulating remyelination of CNS axons in a mammal comprises administering to the mammal the above composition or an amount of the monoclonal antibody, or its mixtures, monomers, active fragments, or derived recombinant antibodies having the ability to bind structures and cells within the CNS, including oligodendrocytes. Treating or preventing a demyelinating disease of the CNS in a mammal comprises administering to the mammal the above composition or an amount of the monoclonal antibody, or its mixtures, monomers, active fragments, or derived recombinant antibodies having the ability to bind structures and cells within the CNS, including oligodendrocytes, and to stimulate remyelination of axons of the CNS. The mammal is a human being having multiple sclerosis, or a human of domestic animal with a demyelinating disease, or a disease or other injury or dysfunction of the CNS. ACTIVITY - CNS-Gen. No biological data given. MECHANISM OF ACTION - Gene therapy. USE - The composition and methods are useful for promoting CNS remyelination or for treating demyelinating diseases as well as other CNS diseases that are of viral, bacterial or idiopathic origin, including neural dysfunction caused by spinal cord injury. ADMINISTRATION - The composition is given at a dose of about 500 ng-600 mug, or about 1.25-2.5 mug/kg. Administration can be intravenous, intraperitoneal, intrathecal, subcutaneous, sublingual, intramuscular, rectal, respiratory, or nasopharyngeal delivery (all claimed). EXAMPLE - No relevant example given. (67 pages)

2/AB/9 (Item 2 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

0337620 DBR Accession Number: 2004-09912 PATENT
New human immunoglobulin M antibody for treating or preventing a demyelinating disease of the central nervous system in a human or domestic animal, such as multiple sclerosis - antibody production via cell culture for use in disease therapy
AUTHOR: RODRIGUEZ M; MILLER D J; PEASE L R
PATENT ASSIGNEE: MAYO FOUND 2003
PATENT NUMBER: US 20030185827 PATENT DATE: 20031002 WPI ACCESSION NO.:

2004-119219 (200412)
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ABSTRACT: DERWENT ABSTRACT: NOVELTY - An antibody (I) produced by injecting an immunocompetent host with an antibody peptide, and harvesting the antibody, where the peptide comprises a sequence (S1) of 113, 110, 124, or 133 amino acids, given in the specification, or active fragments, is new. DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) stimulating remyelination of central nervous system (CNS) axons in a mammal comprising administering a monoclonal antibody, or mixtures, monomers, active fragments, or recombinant antibodies derived from it, characterized by their ability to bind structures and cells within the CNS, including oligodendrocytes; (2) stimulating the proliferation of glial cells in CNS axons in a mammal comprising administering a monoclonal antibody, or mixtures, monomers, active fragments, or recombinant antibodies derived from it, characterized by their ability to bind structures and cells within the CNS; (3) treating or preventing a demyelinating disease of the CNS in a mammal comprising administering a monoclonal antibody, or mixtures, monomers, active fragments, or recombinant antibodies derived from it, characterized by their ability to bind structures and cells within the CNS, and to stimulate remyelination of axons of the CNS; (4) stimulating, in vitro, the proliferation of glial cells from mixed cell culture comprising: (a) culturing a mixed cell culture containing glial cells to proliferate cells; (b) introducing into the mixed culture, a monoclonal antibody, or mixtures, monomers, active fragments, or recombinant antibodies derived from it, characterized by their ability to bind structures and cells within the CNS, including oligodendrocytes, to produce a monoclonal-treated mixed culture; (c) maintaining the culture of (b) to allow proliferation of the cells; and (d) harvesting the glial cells from the mixed culture; (5) stimulating remyelination of CNS axons in a mammal comprising: (a) culturing glial cells; (b) introducing into the cell culture, a monoclonal antibody capable of stimulating the cells to exhibit a calcium (Ca2+) peak, or mixtures, monomers, active fragments, or recombinant antibodies derived from it, the autoantibodies characterized by their ability to bind structures and cells within the CNS, including oligodendrocytes, to produce a treated glial cell culture; (c) maintaining the cell culture of (b) for proliferation of treated cells; (d) harvesting the treated cells from the culture to obtain glial cells; and (e) introducing the glial cells of (d) into the CNS of the mammal; (6) a DNA sequence or degenerate variant of it, which encodes an antibody, or a peptide analog, hapten, or active fragment of it, where the DNA sequence consists of: (i) a sequence encoding a protein having S1; or (ii) a sequence that hybridizes to (i); (7) a recombinant DNA molecule comprising (6); (8) a probe capable of screening for the antibody, peptide analog, hapten, or active fragment, in alternate species, prepared from (6); (9) a unicellular host transformed with (7); (10) an assay for screening drugs and other agents for the ability to modulate the production or mimic the activities of mAB **sHIgM22**, sHIgM46, or combinations of them, comprising: (a) culturing an observable cellular test colony inoculated with a drug or agent; (b) harvesting a supernatant from the colony; and (c) examining the supernatant for the presence of the mAb, where an increase or decrease indicates the ability of the drug to modulate the activity of the mAb, where the mAb can induce remyelination, bind to neural tissue, promote Ca2+ signaling with oligodendrocytes, and promote cellular proliferation of glial cells; (11) a test kit for demonstrating the presence of **sHIgM22**, sHIgM46, or combinations comprising the antibody, a specific binding

partner of the antibody, other reagents, and directions for use of the kit, where the antibody or specific binding partner are detectably labeled; (12) a recombinant virus transformed with (7); (13) a vector comprising (7); (14) a host vector system for the production of a polypeptide which comprises (13) in a host cell; (15) obtaining a purified polypeptide comprising: (a) introducing (13) into a host cell; (b) culturing the cell to produce the polypeptide; (c) recovering the polypeptide; and (d) purifying the polypeptide; (16) imaging a portion of the CNS comprising administering (I), labeled with a detectable label or imaging agent; and (17) diagnosing or monitoring demyelination and/or remyelination of the CNS comprising using (16). BIOTECHNOLOGY - Preferred Antibody: (I) Is monoclonal, polyclonal, or chimeric (bispecific). In (1), (2) and (3), the monoclonal antibody is of the immunoglobulin (Ig)M subtype. In (1) - (5), it is a human antibody and is mAb **sHIgM22** (**LYM 22**), sHIgM46 (LYM46) (both preferred), ebvHIgM MSI19D10, ebvHIgM CB2b-G8, MSI10E10, or mixtures, monomers, active fragments, binding partners or recombinant antibodies of them. The light and heavy chains of **SHIgM22** (**LYM22**) have sequences of 110 and 113 amino acids, respectively. The light and heavy chains of sHIgM46 (LYM46) have sequences of 133 and 124 amino acids, respectively. The monoclonal antibody has a sequence which corresponds to S1 or active fragments. In (4), the mixed culture is obtained from rat optic nerve or rat brain. Preferred Nucleic Acid: In (7), the DNA sequence is operatively linked to an expression control sequence which is selected from the early or late promoters of simian virus (SV40) or adenovirus, the lac, trp, TAC, or TRC system, the major operator and promoter regions of phage lambda, the control regions of fd coat protein, the promoter for 3-phosphoglycerate kinase, the promoters of acid phosphatase, or the promoters of the yeast alpha-mating factors. Preferred Host: The host is an Escherichia coli, Pseudomonas, Bacillus, Streptomyces, a yeast, Chinese Hamster Ovary, R1.1, B-W, L-M, COS 1, COS 7, BSC1, BSC40, or BMT10 cell, or is a plant, insect, or human cell in tissue culture. ACTIVITY - Nootropic; Neuroprotective; Antiviral; Antibacterial; Vulnerary. No suitable biological data is given. MECHANISM OF ACTION - Cell therapy; Vaccine; Gene therapy. USE - (I) Is used to stimulate remyelination of CNS axons, and to stimulate the proliferation of glial cells in CNS axons, optionally in vitro. (I) Is used to treat or prevent a demyelinating disease of the CNS in a human or domestic animal, such as multiple sclerosis, or a disease, other injury or dysfunction of the CNS, preferably the mammal is a mouse infected with Strain DA of Theiler's murine encephalomyelitis virus. (I) Is used to treat a spinal cord injury. (I) Is also used to screen drugs and other agents for the ability to modulate the production or mimic the activities of (I). (I) Can be used to image a portion of the CNS which can be used to diagnose or monitor demyelination and/or remyelination of the CNS (all claimed). ADMINISTRATION - Administration is by intravenous, intraperitoneal, intrathecal, subcutaneous, sublingual, intramuscular, rectal, respiratory or nasopharyngeal routes. Dose of monoclonal antibody is 0.5 - 400 mg/kg. IgM is administered at a dose of 0.5 - 2 g/kg (all claimed). EXAMPLE - No suitable example is given.(159 pages)

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